Appln. No.: 10/550,923

Amendment Dated April 29, 2008

Reply to Office Action of December 31, 2007

## **Amendments to the Specification:**

Please replace the paragraph, beginning at page 4 line 4, with the following rewritten paragraph:

In certain embodiments of the invention, nanometer-sized colloids possessing a desired surface chemistry and charge are used as the template starting material. Using silica colloids as a non-limiting example, the inventors have demonstrated the feasibility of the invention. The silica colloids obtained by this technology have a typical diameter of about 10-5000 nm and preferably a monodispersed narrow size distribution. The amine group on the colloidal particle surface can be coupled to other functional groups, synthetic or natural polymers, and biomolecules such as, for example, genes, proteins, growth factors and other bio-functional moieties by, for example, covalent bonding, lidandligand-substrate binding and electrostatic adsorption. Binding of various molecules to the nanoparticle can be repeated to build up multiple layers of functionality of very precise thickness desired in various applications (e. g., tissue engineering). Upon achieving an appropriate functionalization or coating, other bioactive layers such as, for example, hydroxyapatite may be deposited to enhance response to bone cells. Once the desired biomimetic nano-structure is evolved, these biomimetic nanoparticles can be dispersed in a polymeric matrix and then formed into gels, fibers, meshes and solids to form the three dimensional construct of the invention. It can be formed into shapes by standard polymer forming processes, such as extrusion, molding, pouring, electrospinning, spin coating, stamping, 3 dimensional printing and other methods known in the art. Alternatively, such biomimetic nanoparticles can be used to coat surfaces of biocompatible constructs to impart or enhance their biofunctionality.

Please replace the paragraph, beginning at page 6 line 20, with the following rewritten paragraph:

The invention flows from the discovery that a three-dimensional construct comprising a nanoparticle dispersed in a polymeric matrix, wherein the nanoparticle is coated with a monomolecular layer comprising biological information can be used to present this information to a cell or a tissue in a predictable and controllable manner. Inventors have discovered that nanoparticles can be constructed to have a desirable size and characteristics and further applied

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in combination with various materials and surfaces to a <del>call cell</del> or a tissue to cause a desired effect.

Please replace the paragraph, beginning at page 7 line 13, with the following rewritten paragraph:

As a non-limiting example, nanoparticles of inorganic oxides such as silicon oxide were prepared by a sol-gel process and functionalized to bear amine groups covalently bound to the surface of nanoparticles and thereby imparting a positive charge. Next, a molecular layer of biocompatible synthetic polymer bearing an opposite charge (negative charge), e. g., poly (acrylic acid) was assembled onto the colloidal particles in solution under appropriate pH to render the surface negatively charged. This negatively charged colloidal surface was further modified by a <BR> monomolecular layer of a biologically relevant natural polymer, e.g., collagen via electrostatic assembly to introduce bio-recognition. The layer of collagen can then be then used to bind biomolecules such as, for example, growth factors, peptides, and nucleotides by a non-covalent approach. In addition, such biological layer offers cellular binding sites (e. g., RGD) and a natural surface for deposition of bio-ceramics such as hydroxyapatite.